The Response

1. **Substituted Specification**

Applicants are submitting herewith a substitute specification, a marked-up copy of the application to show changes made, and a Request for the Substitute Specification. The Examiner is respectfully requested to enter the Substitute Specification.

2. **Objection to the Specification**

The specification is objected to because of informalities. Applicants have amended the specification to insert the requisite Sequence ID numbers. Therefore, the objection to the disclosure should be withdrawn.

3. **Claim Objection**

Claims 6 and 7 are objected to as being in improper form. Applicants have amended Claims 6 and 7 to depend on Claim 1 only. Therefore, Applicants request the Examiner to withdraw the objection to Claims 6 and 7.

4. **Rejections under 35 U.S.C. § 112, First Paragraph: Enabling**

Claims 1-5 and 8 are rejected under 35 U. S. C. 112, first paragraph. The Examiner states that the specification, while being enabling for a method of determining the presence of overrepresentations of chromosomal segments in a population of immortalized cells derived from a cell line, does not reasonably provide enablement for the detection and determination of any type of "change" in any cell.

To further prosecution, Applicants have amended Claim 1 to recite that "a process for detecting chromosomal overrepresentation in cells."

Therefore, the §112, first paragraph enabling rejection of Claim 1 and its dependent claims 2-5 and 8 should be withdrawn.

5. **Rejections under 35 U.S.C. § 112, First Paragraph: Written Description**

Claims 1-5 and 8 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner states that "the specification has been found to support the detection of changes in chromosomal number, but not the detection of any change in the DNA."

To further prosecution, Applicants have amended Claim 1 to recite that "a process for detecting chromosomal overrepresentation in cells." Therefore, the §112, first paragraph, written description rejection of Claim 1 and its dependent Claims 2-5 and 8 should be withdrawn.

6. **Rejections under 35 U.S.C. §112, Second Paragraph**.

Claim 1 is rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that Claim 1 is indefinite with respect to what constitutes "normal cells". The rejection is traversed in parts and overcome in parts in view of the claim amendment.

Claim 1 is directed to a process for detecting chromosomal overrepresentation in cells. In the specification at page 2, "normal cells" are defined as cells of any kind and origin, which have no known numerical changes in its DNA. The dictionary definition of "numerical" is of or relating to numbers. "Numerical changes in DNA" means extra numbers of DNA, or additional copies of DNA, or chromosomal overrepresentation. Normal cells mean cells without chromosomal overrepresentation. Applicants submit that both "numerical changes" and "normal cells" are clearly defined by its ordinary meaning and the specification.

In view of the above amendments, Applicant respectfully requests the withdrawal of rejections under 35 U.S.C. §112, second paragraph.

7. **Rejections under 35 U.S.C. §103(a)**.

Claim 8 is rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Worton, *et al.*, in view of Batt, *et al.*

Worton, *et al.*, describe a method in which amplified HRR cDNA copies of normal and mutated HHR genes are compared and sequence discrepancies are detected. As these sequence discrepancies do not comprise numerical changes of the HRR gene, Worton, *et al.*, do not teach or suggest a method for detecting chomosomal overrepresentation in cells.

Batt, *et al.*, disclose a method for detecting Bovine Herpes-virus-1 (BHV-1) infection using BHV-1 specific oligonucleotides as primers to amplify a particular region of the genome of BHV-1. Batt, *et al.*, also do not teach or suggest a process for detecting chromosomal overrepresentation in cells.

Consequently, the combination of Worton, *et al.*, and Batt, *et al.*, does not give any hint to a kit for carrying out the process for detecting chromosomal overrepresentation in cells (Claim 8). Therefore, the §103(a) rejection over Worton and Batt should be withdrawn.

CONCLUSION

It is now believed that the claims are in condition for allowance and advancement as such is earnestly requested. Should any questions arise in connection with this

submission which may be resolved by a telephonic interview, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

AMENDMENTS

In the Claims

1. (Twice Amended) A process for detecting [changes] chromosomal overrepresentation in cells [DNA], comprising the following steps:

(a) isolating DNAs from cells which have no known numerical changes in their DNAs, and amplifying the DNAs by means of a PCR method using tag primers;

(b) hybridizing [of] cells under study *in situ* with the amplified DNAs from (a);

(c) amplifying DNAs from the *in situ* hybridized cells from (b) by means of a PCR method using the tag primers from (a);

(d) cohybridizing the DNAs from (a) and (c) to metaphase chromosome spreads from normal cells under suppression hybridization conditions; and

(e) identifying numerical changes in the amplified DNAs from (c).

2. (Amended) The process according to claim 1, [characterized in that] wherein the cells under study originate from tumors.

3. (Amended) The process according to claim 1, [characterized in that] wherein the cells under study originate from the blood of pregnant persons.

4. (Twice Amended) The process according to claim 2 or 3, [characterized in that] wherein the cells under study are those of a cell population or single cells.

5. (Amended) The process according to [any one of claims 1 to 4] claim 1, [characterized in that] wherein the cells under study have an interphase nucleus.

6. (Amended) The process according to [any one of claims 1 to 5] claim 1, [characterized in that] wherein the tag primers are degenerative primers.

7 (Amended) The process according to [any one of claims 1 to 6] claim 1, [characterized in that] wherein the identification from (d) comprises a "Comparative Genomic Hybridization" (CGH) method.

8. (Twice Amended) A kit for carrying out the process according to [any one of claims 1 to 7] claim 1, comprising the following components:

(a) DNAs flanked by tag primers that are amplified from cells that have no known numerical changes in their DNAs;

(b) tag primers; and

(c) auxiliary agents for identifying numerical changes in a DNA.